PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 022041-000700PC	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/07785	International filing date *(day/month/year)* 14 March 2003 (14.03.2003)	Priority date *(day/month/year)* 15 March 2002 (15.03.2002)

International Patent Classification (IPC) or national classification and IPC

IPC(7): C12Q 1/68; C12P 19/34, , 21/06; C07H 21/04 and US Cl.: 435/6, 91.21, 69.1; 536/24.33

Applicant

ARCTURUS ENGINEERING, INC.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09 October 2003 (09.10.2003)	18 August 2005 (18.08.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Suryaprabha Chunduru Telephone No. 703-308-0196

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/07785

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-54 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 55-60, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-8, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/07785

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 15-19, 30-37

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 15-19 and 30-37

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-14, 20-29, 38	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-14, 20-29, 38	NO
Industrial Applicability (IA)	Claims 1-14, 20-29, 38	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-14, 20-29, 38 lack an inventive step under PCT Article 33(3) as being obvious over Baugh et al. (Nucleic Acids Res., Vol. 29, No. 5, e 29: 1-9, 2001) in view of Smith et al. (USPN. 6,027,945).

Baugh et al. teach a method for synthesizing a double-stranded cDNA and detection of rare mRNA wherein Baugh et al. disclose that the method comprises (a) synthesizing a pool of first cDNA strands in a first reaction mixture comprising reverse transcriptase, an RNA template and a first strand primer that is complementary the RNA template (see page 2, column 1, paragraph 2); (b) removing the RNA template by RNase H and (c) producing a pool of double-stranded cDNA in a reaction mixture comprising processive DNA polymerase, a DNA ligase, a pool of single stranded cDNA strands as template and random primers (see page 2, column 1, paragraph 2, column 2, paragraph 1); (d) synthesizing an amplified complementary RNA (antisense RNA) in a third reaction mixture comprising RNA polymerase and the pool of double-stranded cDNA (see page 2, column 1, paragraph 2). Baugh et al. also teach that the method comprises (i) oligo dT-RNAP primer comprising a single stranded oligonucleotide (about 24 nucleotide) with a first and a second segment, wherein second segment comprises recognition site for an RNA polymerase (see page 2, column 1, paragraph 2); RNA polymerase is selected from T7 RNA polymerase (see page 2, column 1, paragraph 2). However Baugh et al. did not teach purifying the amplification product with a solid phase.

Smith et al. teach a method of isolating biological target materials (nucleic acids) using a silica magnetic solid particles, wherein Smith et al. teach that the method comprises providing a solid phase (silica) and combining the solid phase with the biological material and isolating the target-solidphase complex and recovering the biological material from the solid phase (see col. 5, line 1-30).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of amplifying rare mRNA with random primers as taught by Baugh et al. with a step of isolating the nucleic acid as taught by Smith et al. to achieve expected advantage of developing a sensitive and enhanced method of isolating purified nucleic acids. An ordinary practitioner would have been motivated to combine the teaching of Baugh et al. with the step of isolating the nucleic acids as taught by Smith et al. because incorporating the step of isolating nucleic acids would improve the quality of the amplified nucleic acid and facilitate isolation of purified nucleic acids.